

**WHAT IS CLAIMED IS:**

1. An orally administrable pharmaceutical composition for preventing the decrease in the bioavailability of a drug after food intake, wherein the drug's bioavailability is decreased by interaction with digestive enzymes or food ingredients after food intake, comprising:

- i) said drug; and
- ii) a pharmaceutically acceptable bioadhesive polymer.

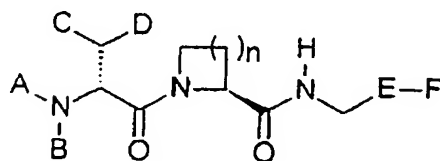
2. The composition of Claim 1, which is in the form of granule or pellet.

3. The composition of Claim 1, further comprising one or more pharmaceutically acceptable additives.

4. The composition of Claim 3, wherein one or more pharmaceutically acceptable additives are selected from the group consisting of solubilizing agent, osmotic agent, disintegrator, lubricant, binder, filler, or mixture thereof.

5. The composition of Claim 1, wherein the drug is a thrombin inhibitor.

6. The composition of Claim 5, wherein the thrombin inhibitor is a compound of the following formula:



(I)

, wherein n is 1, 2, or 3;

A is hydrogen, alkyl, C<sub>3-7</sub>cycloalkyl, aryl, -SO<sub>2</sub>R<sup>1</sup>, -SO<sub>3</sub>R<sup>1</sup>, -COR<sup>1</sup>, -CO<sub>2</sub>R<sup>2</sup>, PO(OR<sup>1</sup>)<sub>2</sub>, -(CH<sub>2</sub>)<sub>m</sub>CO<sub>2</sub>R<sup>1</sup>, -(CH<sub>2</sub>)<sub>m</sub>SO<sub>2</sub>R<sup>1</sup>, -(CH<sub>2</sub>)<sub>m</sub>SO<sub>3</sub>R<sup>1</sup>, or -(CH<sub>2</sub>)<sub>m</sub>PO(OR<sup>1</sup>)<sub>2</sub>,  
 wherein R<sup>1</sup> is hydrogen, C<sub>1-6</sub>alkyl, C<sub>3-7</sub>cycloalkyl, aryl, -(CH<sub>2</sub>)<sub>m</sub>aryl, or -NR<sup>3</sup>R<sup>4</sup>,  
 R<sup>2</sup> is C<sub>1-6</sub>alkyl, C<sub>3-7</sub>cycloalkyl, aryl, -(CH<sub>2</sub>)<sub>m</sub>aryl, or alkenyl,

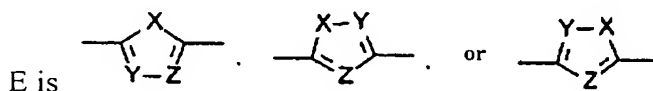
m is 1, 2, or 3,

wherein aryl is unsubstituted or substituted phenyl or 5-6 membered aromatic heterocyclic ring,

$R^3$  and  $R^4$  are independently of each other hydrogen,  $C_{1-6}$ alkyl,  $C_{3-7}$ cycloalkyl;

5 B is hydrogen or  $C_{1-6}$ alkyl;

C and D are independently of each other hydrogen, unsubstituted or substituted phenyl with one or two substituents selected from  $C_{1-4}$ alkyl,  $C_{1-4}$ alkoxy,  $CF_3$ , methylenedioxy, halogen, hydroxy, or  $-NR^3R^4$ ,  $C_{3-7}$ cycloalkyl, or a 5-6 membered heterocyclic ring system which may be saturated or unsaturated, and which consists of  
10 carbon atoms and 1-3 heteroatoms selected from the group consisting of N, O, and S;



, wherein X is S, O, or  $NR^5$ ,

Y and Z are independently of each other N or  $CR^6$ ,

wherein  $R^5$  is hydrogen or  $C_{1-4}$ alkyl, and  $R^6$  is hydrogen, halogen,  $CF_3$ , or  $C_{1-4}$ alkyl; and  
15

F is  $-C(NH)N(R^7)_2$ ,  $-C(NH_2)NN(R^7)_2$ ,  $-C(NH_2)NOH$ , or  $-CH_2NH(R^7)_2$ ,

wherein  $R^7$  is same or different, and is hydrogen,  $C_{1-4}$ perfluoroalkyl,  $C_{1-4}$ alkyl, or a pharmaceutically acceptable salt thereof.

20 7. The composition of Claim 6, wherein the compound of formula (I) is (2S)-N-{5-[amino(imino)methyl]-2-thienyl}methyl-1-[(2R)-2-[(carboxymethyl)amino]-3,3-diphenylpropanoyl]-2-pyrrolidinecarboxamine.

8. The composition of Claim 5, for preventing or treating thrombosis, myocardial  
25 infarction, unstable angina, deep vein thrombosis, pulmonary thrombosis, stroke, or disorders associated with excessive thrombin.

9. The composition of Claim 5, wherein the thrombin inhibitor is selected from the group consisting of S-18326, S-31922, R-Piq-Pro-Arg-H, and melagatran.

10. The composition of Claim 1, wherein the bioadhesive polymer is selected from the group consisting of polyethylene oxide, cellulose ether, polyvinylpyrrolidone (PVP), acrylic acid polymer, mucin, agar, gelatin, pectin, alginate, natural gum, and their mixture.

5

11. The composition of Claim 10, wherein the bioadhesive polymer is selected from the group consisting of Polyox, Carbopol, hydroxypropyl methylcellulose, and their mixture.

10

12. The composition of Claim 1, which is enteric coated.

13. The composition of Claim 12, which is enteric coated with hydroxypropyl methylcellulose phthalate, cellulose acetate phthalate, carboxymethyl ethylcellulose, methacrylic acid methacrylate copolymer, or mixture thereof.

15

14. The composition of Claim 11, which is further film coated on the enteric coating.

15. The composition of Claim 14, which is film coated with hydroxypropyl methylcellulose, hydroxyethyl cellulose, hydroxypropyl cellulose, methylcellulose, ethylcellulose, acrylic acid methacrylic acid ester copolymer, or mixture thereof.

20

16. An orally administrable formulation prepared from the composition of any one of Claims 1 to 15.

25

17. The formulation of Claim 16, which is in the form of soft or hard capsule, or tablet.

18. The formulation of Claim 16, prepared by adding one or more pharmaceutically acceptable additives to the composition.

30

19. The formulation of Claim 18, wherein one or more pharmaceutically acceptable additives are selected from the group consisting of solubilizing agent, osmotic agent, disintegrator, lubricant, binder, filler, and their mixture.

- 5 20. The formulation of Claim 18, which comprises:
- i) 10 to 90 parts by weight of a thrombin inhibitor;
  - ii) 10 to 99 parts by weight of a bioadhesive polymer; and
  - iii) 1 to 1000 parts by weight of a solubilizing agent, an osmotic agent, or a disintegrator.

10

21. A method for preventing the decrease in the bioavailability of a drug after food intake, which comprises using the composition of any one of Claims 1 to 15.